state. In addition, a substantial number of children with the disorder have significant problems as adolescents, with educational retardation and antisocial behavior, including substance abuse. Serious antisocial behavior is present in 10% to 50% of different samples of children with the ADDH syndrome when they reach adolescence. Almost all of these children who have significant substance abuse manifest other forms of antisocial behavior, and almost all of those children with the syndrome who show antisocial behavior in adolescence have ADDH residual state.

These findings are also true of adult samples. In addition, several studies have found high rates of "dysphoric disorders" in adults with the ADDH syndrome.

Psychopharmacologic studies of both adolescents and adults with ADDH indicate that stimulant medication is still effective and does not produce a "stimulating" effect. Sustained attention, impulsivity and motor activity are symptoms most affected by stimulants. Results of relatively long-term multimodality treatment studies suggest that multimodality intervention is quite effective in childhood. However, there is little evidence from published studies that treatment *limited to* childhood has any long-term effect in adolescence or adulthood.

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Hormones and Behavior

IT IS NOW well established that behavior influences hormone secretion and, conversely, that altered circulating hormone concentrations can influence behavior.

Altered secretion patterns of many of these hormones have been identified in cases of acute and chronic stress, in psychiatric illnesses including mania, depression and schizophrenia and as a result of drugs that act on the central nervous system—such as neuroleptics, alcohol and opiates. Perhaps most relevant to clinical psychiatry is the use of these hormone changes as tests to aid in the differential diagnosis of certain illnesses and to follow response to treatment. The dexamethasone-suppression test (DST) is the best known of these, having been proposed as a laboratory aid in the diagnosis of endogenous or melancholic depression, the subtype of major depression often requiring somatic treatment (antidepressants, electroconvulsive therapy). In the DST, the synthetic glucocorticoid dexamethasone, usually 1 mg, is given orally about midnight and the serum cortisol concentration is measured at certain times the next day. Dexamethasone normally suppresses adrenocorticotropic hormone and cortisol secretion for a full 24 hours, whereas 30% to 60% of patients with endogenous depression show an early cortisol escape, most likely on the basis of increased hypothalamic driving of the anterior pituitary-adrenal cortex. The practical application of the DST as a diagnostic aid has been hampered by issues of varying sensitivity (percentage of index cases with abnormal—that is, true-positive—DST results) and specificity (percentage of comparison cases with normal—that is, true-negative—DST results) and interference in the test results by a number of drugs and medical conditions. At present, the DST appears to be most useful in following the adequacy of treatment. Those patients with an abnormal pretreatment DST response who improve symptomatically with treatment but continue to have an abnormal test result are at greater risk for relapse than those patients whose DST findings revert to normal. The former patients may require electroconvulsive therapy in addition to pharmacotherapy for a full remission. In some patients with recurrent depression, the DST findings may again become abnormal several weeks before a clinically evident relapse. This is a promising aspect of the test that requires further study.

Similar limitations apply to another widely used neuroendocrine test for endogenous depression, the thyrotropin-releasing hormone (TRH) stimulation test, in which TRH is given intravenously and the serum thyrotropin (thyroid-stimulating hormone) level is measured. A thyrotropin response below a certain criterion level is considered blunted and thus abnormal. At best, both the DST and the TRH test should be applied only in selected cases and with full cognizance of their limitations both generally and in specific patients. They are neither screening tests nor substitutes for a careful clinical assessment.

Triiodothyronine, or T_3, the metabolically active thyroid hormone, may be a useful therapeutic adjunct to tricyclic antidepressants in some endogenously depressed patients who are refractory to the latter medications alone, even though such patients do not have clinically evident hypothyroidism. Presumably, the T_3 sensitizes postsynaptic neurotransmitter receptors in the central nervous system, similar to the mechanism proposed for the adjunctive effect of lithium in persons with tricyclic-resistant depression.

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Positron Emission Tomography in Psychiatric Disorders

POSITRON EMISSION TOMOGRAPHY (PET) is a new computerized tomographic technique that allows the visualization of brain structures relative to their uptake of radioactive tracers. Tracer substances are manufactured that contain unstable atoms which decay to emit a positron. This positron in turn annihilates with an electron to produce gamma particles. This radiation is picked up by sensors and a computer program is used to reconstruct a picture based not on x-ray density but on the local concentration of the tracer. PET scans thus permit us

to examine the biochemical functions of the brain in which the various positron-labeled tracer substances are involved.

The PET scan presently is strictly a research tool, though it may have applications in clinical psychiatry in the future. To date most studies have involved substances like water ^{15}O to look at blood flow or fluorodeoxyglucose ^{18}F to look at glucose metabolism. A few studies have been done using labeled drugs, most notably spiroperidol, which binds to and thus allows localization of dopamine receptors.

PET studies of glucose metabolism are already yielding interesting findings in cases of major psychiatric illness. In patients with chronic schizophrenia, glucose metabolism in the frontal lobes appears low when compared with that of posterior brain regions. This pattern is the reverse of that seen in normal persons. In mood disorders one group reports that patients with bipolar (manic-depressive) depression have low metabolic rates in all supratentorial brain structures when compared with normal persons, patients with bipolar depression who are in a manic state and even those with unipolar depression. In contrast, patients with unipolar depression show a decrease in the metabolic rate of the caudate nucleus relative to that of the person's brain as a whole. In another study, using water ^{15}O to study blood flow, those patients with panic disorder in whom an infusion of sodium lactate causes a panic attack were shown to have a decrease in blood flow to the left hippocampal gyrus compared with that on the right. These two interesting studies await replication.

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Use of Carbamazepine in Mood Disorders

CARBAMAZEPINE (TEGRETOL) is used extensively to treat partial complex (psychomotor or temporal lobe) and major motor (grand mal) seizures. In the past few years, carbamazepine has been shown to have value in treating cases of bipolar (manic-depressive) disorders. In studies carried out first in Japan and then in this country this drug has been remarkably effective both in treating patients with manic episodes and for maintenance to prevent recurrences. Its efficacy is on a par with that of lithium carbonate and many patients who do not respond to or cannot tolerate lithium can be effectively treated with carbamazepine. At present, it is usually only used in such patients. Carbamazepine may be effective in treating patients with depression, both bipolar and unipolar, though this is less well documented than its effects in cases of mania.

Treatment begins with 100 or 200 mg given twice a day, which increases, as patient tolerance permits, to a total of 600 to 1,600 mg a day (average dose about 1,000 mg a day). Carbamazepine blood concentrations do not correlate with therapeutic response in bipolar illness. Carbamazepine is compatible with most other psychiatric drugs. Some patients have required treatment with both carbamazepine and lithium to get an adequate response, though there are reports of occasional central neurotoxicity.

Carbamazepine is closely related to the tricyclic antidepressants and should not be added to the regimen of a patient already taking a monoamine-oxidase inhibitor. As with other tricyclics, monoamine-oxidase inhibitors can be added once a person is taking carbamazepine.

Many physicians have been unduly frightened about carbamazepine because of early reports of aplastic anemia occurring. Most of these cases were in elderly patients with numerous medical problems being treated with many drugs. Despite the increasing use of carbamazepine by neurologists and psychiatrists, there has not been a corresponding increase in cases of aplastic anemia related to its use. Side effects with the use of carbamazepine consist of those that can be seen with tricyclic antidepressants, but, in addition, there seems to be an increased incidence of dizziness (often true vertigo), pruritic rash and a mild lowering of the leukocyte count. Liver toxicity rarely occurs.

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Update on Electroconvulsive Therapy

ELECTROCONVULSIVE THERAPY remains a viable and important treatment in psychiatry. In California, for example, some 2,600 patients receive it each year (in spite of the strict legal requirements in the state).

More than a dozen different antidepressants are available in the United States, yet many patients with major depression respond only to electroconvulsive treatment. Response rates in the order of 70% to 90% have been shown. In some cases of severe life-threatening depression or in patients who are severely ill medically, electroconvulsive therapy is the treatment of choice. Manic patients who are not responsive to conventional treatments have about a 90% response rate to this treatment. Although manic exhaustion and depressive inanition were once common causes of death, today they are quite rare. Schizophrenic patients in acute stages who are unresponsive to standard treatments or who have experienced severe side effects, such as agranulocytosis or severe tardive dyskinesia, have a 75% response rate with electroconvulsive therapy. It is extremely safe, with a mortality rate of only 0.2 deaths per 10,000 treatments in California from 1977 to 1983.

There are virtually no absolute medical contraindications to electroconvulsive therapy. Although a brain tumor or a recent myocardial infarction are generally considered contra-